

The Strategy Behind A Lifespan Screen

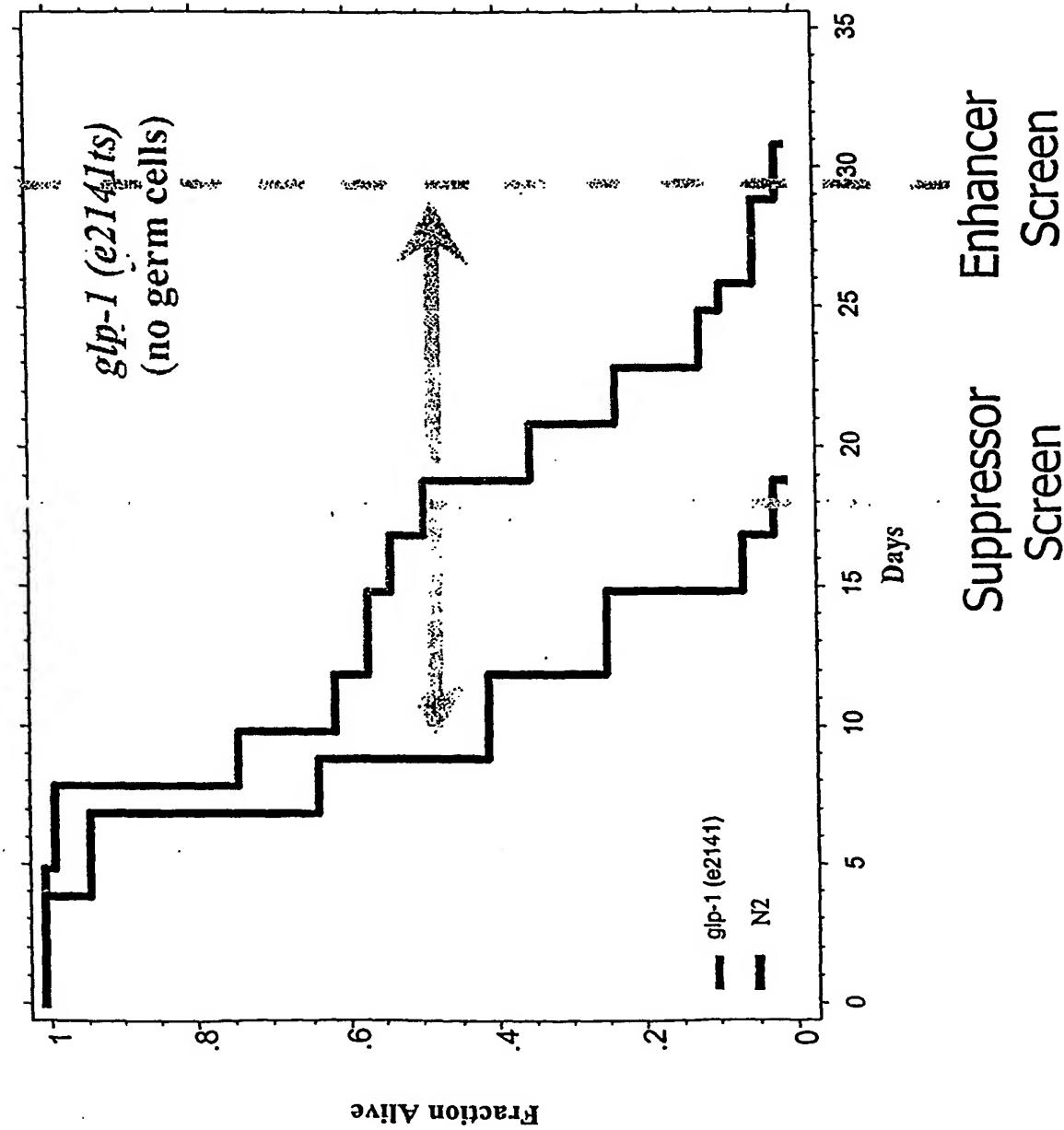


Figure 1

An Insulin Signaling Pathway and Signals from the Reproductive System Regulate Lifespan in *C. elegans*

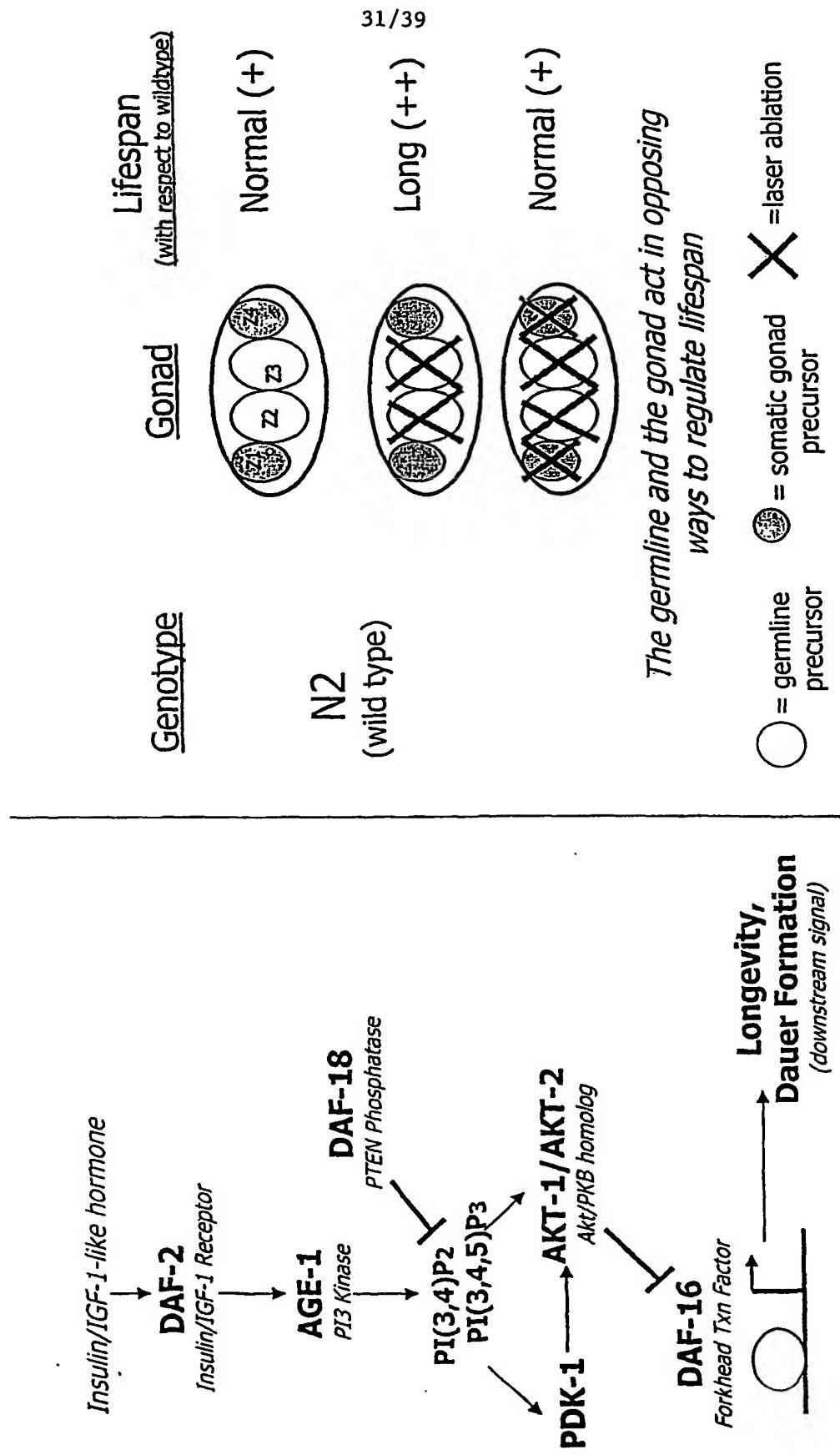


Figure 2

The Reproductive System Modulates Several Genes to Control Aging

Genotype	Gonad	Lifespan (with respect to wildtype)	Genotype	Gonad	Lifespan (with respect to wildtype)
<i>daf-16(-)</i> or <i>daf-12(-)</i> or <i>daf-9(-)</i>		Short (-)	<i>daf-2(-)</i> [strong alleles]		Long (++)
		Short (-) [no change]			Even Longer (+++)
					Even Longer (+++)

The germline signal shortens lifespan through downregulation of *daf-16*, *daf-12*, and *daf-9*

The somatic gonad, but not the germline, extends life through modulation of the *daf-2* insulin pathway.

<i>daf-16(-)</i>		Even Shorter (-)
<i>daf-12(-)</i> or <i>daf-9(-)</i>		Short (-) [no change]

The somatic gonad signal acts through *daf-12* and *daf-9*, yet independently of *daf-16*, to promote longevity.

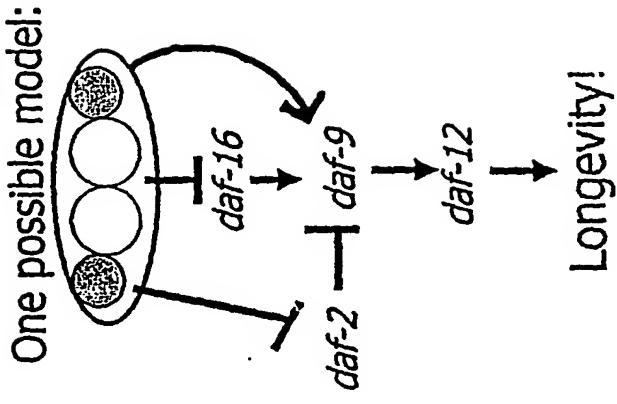
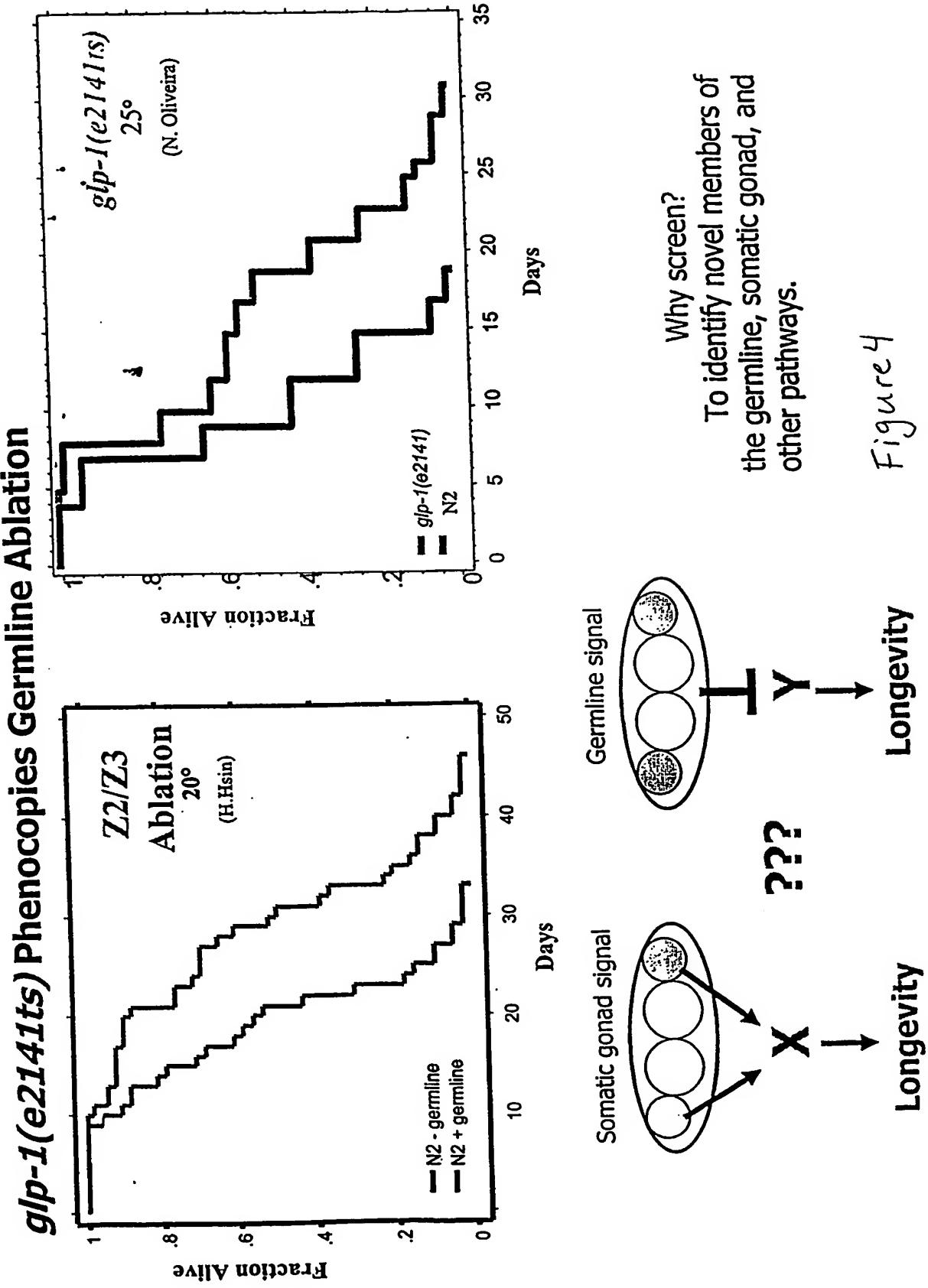


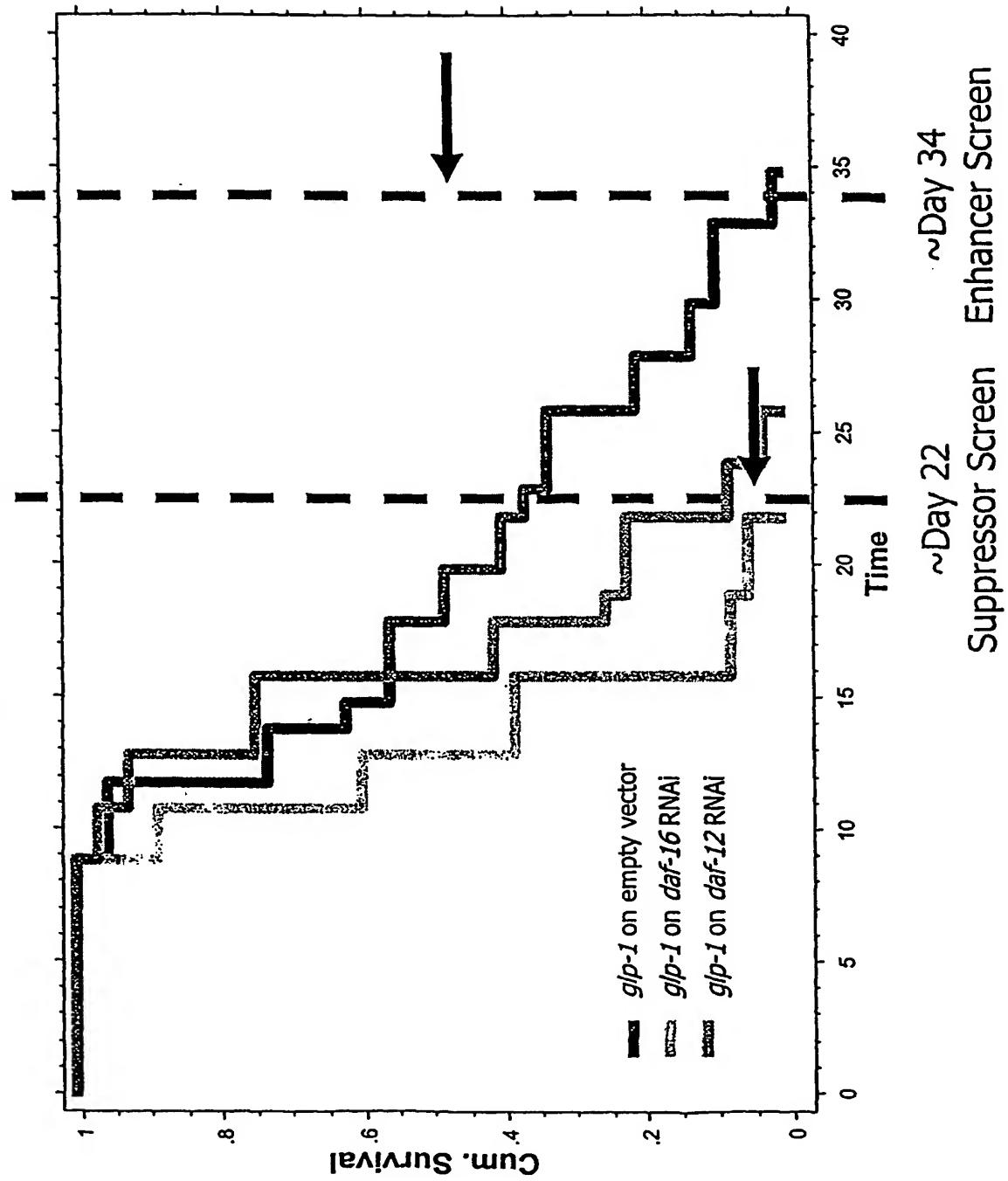
Figure 3

What other genes are involved in this process?

Longevity!

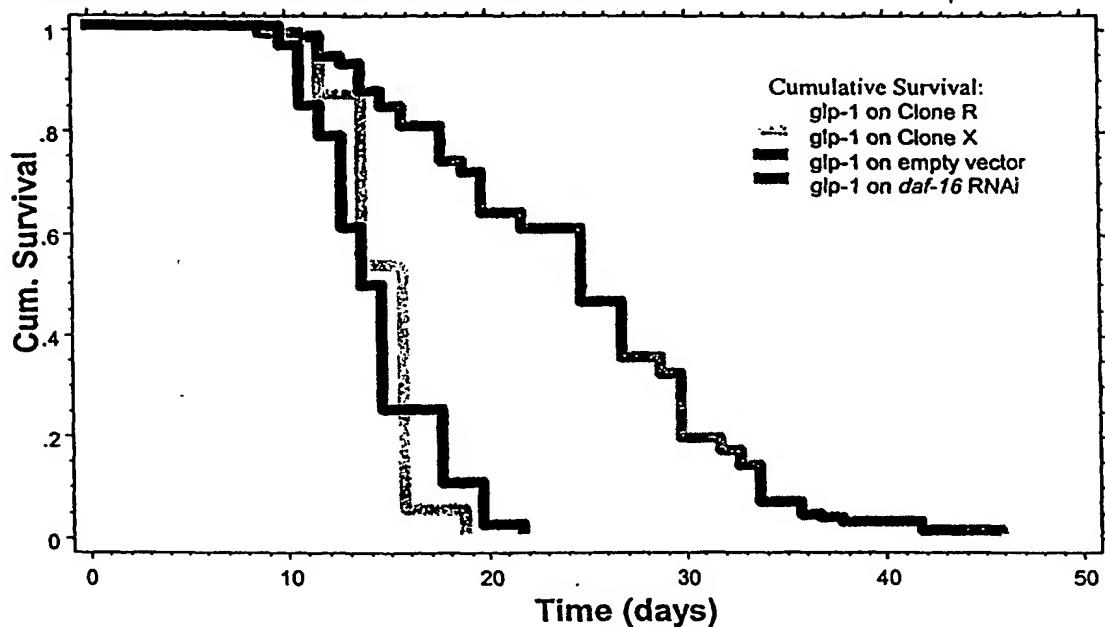
An RNAi Screen for Suppressors and Enhancers of *gfp-1* Lifespan Extension



Strategy for the *g/p-1* screen**Figure 5**

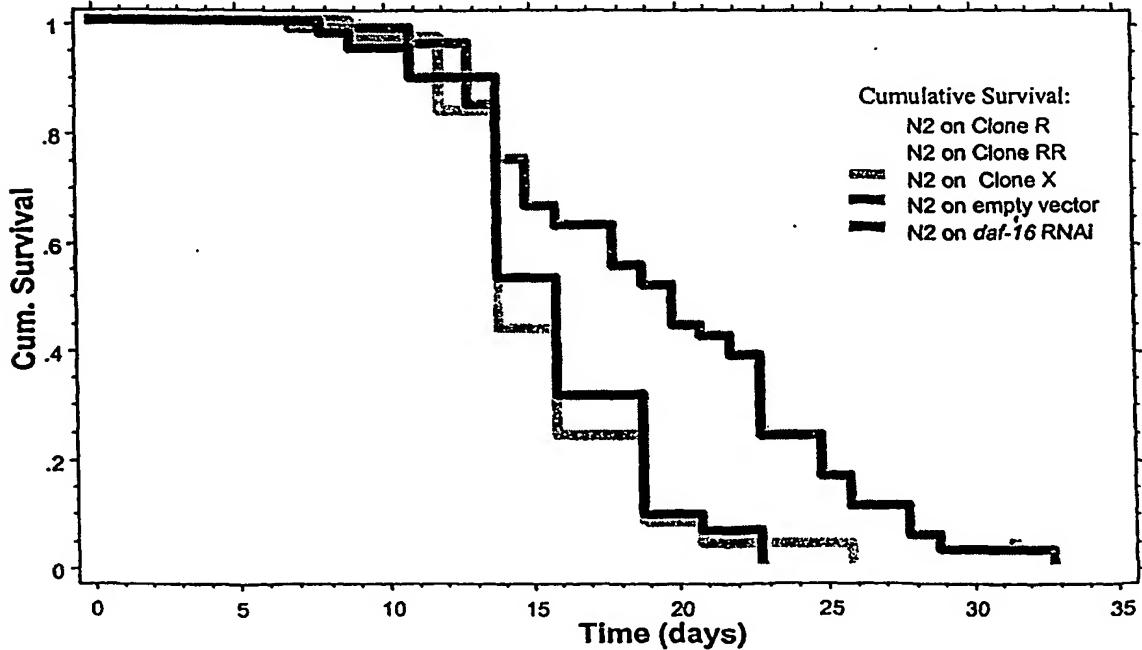
Establishing Specificity: Effects on N2 Longevity

Examples of *glp-1* suppressors:



RNAi Clone R and Clone X suppress *glp-1* longevity to *daf-16* levels

Differential effects on N2 longevity:



Clone R has no effect on N2 lifespan, and Clone X slightly suppresses wild-type lifespan to *daf-16* levels. Clone RR dramatically reduces N2 lifespan,

Figure 6

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Figure 7

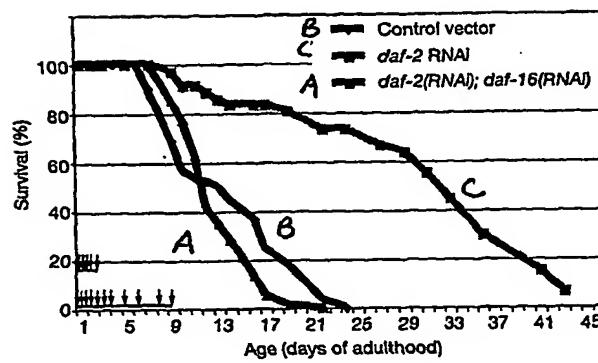
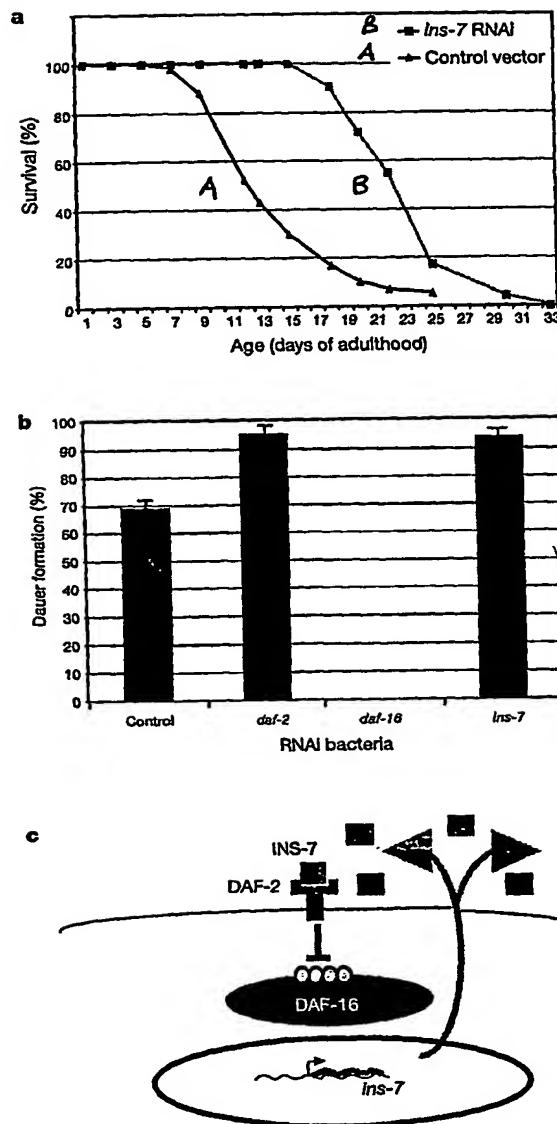


Figure 8



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Figure 9

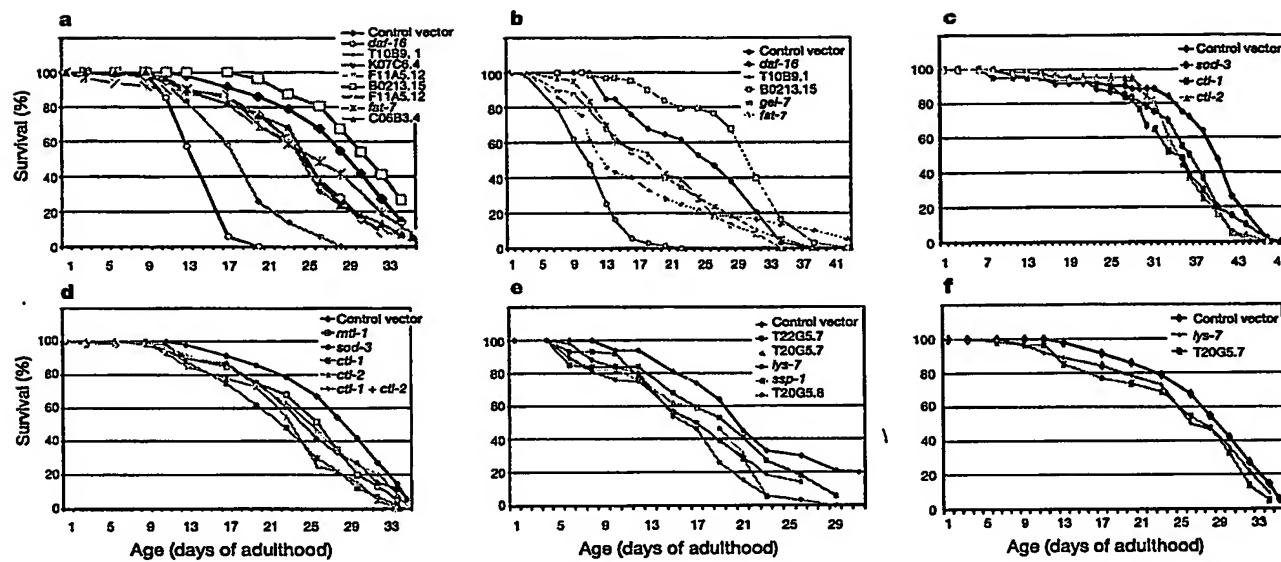


Figure 10

